General

Guideline Title

Overweight and obesity. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents.

Bibliographic Source(s)

Overweight and obesity. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. p. 282-321. [132 references]

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- April 8, 2016 – Metformin-containing Drugs : The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function.

Recommendations

Major Recommendations

Definitions of the levels of the evidence (A, B, C, D) and strength of recommendations are presented at the end of the "Major Recommendations" field.

Note from the National Heart, Lung and Blood Institute (NHLBI) and the National Guideline Clearinghouse (NGC): Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents has been divided into individual summaries covering the major cardiovascular risk factors. In addition to the current summary, the following are available:

- Family history of early atherosclerotic cardiovascular disease
- Nutrition and diet
- Physical activity
- Tobacco exposure
- High blood pressure
- Lipids and lipoproteins
- Diabetes mellitus and other conditions predisposing to the development of accelerated atherosclerosis
- Risk factor clustering and the metabolic syndrome
- Perinatal factors

Conclusions and Grading of the Evidence Review on Treatment of Obesity

- There is good evidence for the effectiveness of combined weight loss programs that included behavior change counseling, negative energy balance through diet, and increased physical activity in addressing obesity in children older than age 6 years with a body mass index (BMI) at or greater than 95th percentile and no comorbidities (Grade A). However, such programs have primarily been shown to be effective in a comprehensive weight loss program or research settings, with only a small number shown to be effective in primary care settings.
- No data were identified on weight loss programs for children younger than age 6 years.
- No single negative energy diet plan was identified from the evidence review. Dietary plans should be determined for each child, based on baseline body size, energy requirements for growth, and physical activity level (Grade D).
- Increasing dietary fiber from corn bran, wheat flour, wheat bran, oat flakes, corn germ meal, or glucomannan does not significantly improve weight loss (Grade A).
- Various diets have been inadequately studied as to their effects on obesity in children and adolescents, including low glycemic-load diets, low-carbohydrate diets, fiber supplements, and protein-sparing modified fasts.
- For children ages 6–12 years:
    - Family-based programs in research settings have been shown to be effective at initiating and sustaining weight loss over a followup of 10 years (Grade A).
    - The greatest weight loss is achieved when parents are the focus of the intervention (Grade A).
- For adolescents:
    - Comprehensive programs in research settings were effective at achieving weight loss in the short term (Grade A).
    - The greatest weight change was achieved when the adolescent was the primary focus of the intervention (Grade B).
    - Behavior change programs that involved peers achieved more sustained weight loss (Grade B).
- In overweight and obese youth, the combination of diet and a specific physical activity intervention that reduced sedentary activity and/or increased physical activity was universally more effective at achieving decreases in weight and BMI, as well as decreases in body fat compared with an isolated diet intervention:
    - In both children and adolescents, exercise training improved weight loss and body composition (decreasing fat mass and reducing visceral fat), decreased insulin resistance (IR), reduced blood pressure (BP), normalized dyslipidemia, and normalized subclinical measures of atherosclerosis (Grade A).
    - In children ages 7–12 years, reduction in sedentary activity, independent of increasing physical activity, produced weight loss (Grade B). In this age group, reductions in sedentary activity were effectively accomplished by rewarding children for time spent being physically active with TV viewing time (Grade B).
    - Girls did not respond as well as boys to combined treatments that both reduced sedentary behaviors and increased physical activity (Grade B).
- For adolescents with or without significant comorbidities, with a BMI greater than or equal to the 95th percentile and for adolescents with a BMI greater than 35 kg/m^2 who have failed a comprehensive lifestyle weight loss program, addition of medication under the care of a physician experienced in managing weight loss with medication can be safe and effective in achieving weight loss with followup of 4–12 months. However, long-term safety and efficacy data are not available:
    - In adolescents with severe obesity and IR, the addition of metformin to a comprehensive lifestyle weight loss program improved fasting insulin and significantly reduced weight and BMI (Grade B). (Metformin is currently approved by the U.S. Food and Drug Administration [FDA] for pediatric patients ages 10 years and older with type 2 diabetes mellitus [T2DM] but is not approved for weight loss for either children or adults.)
    - For obese adolescents older than age 12 years, the addition of orlistat to a comprehensive lifestyle weight loss program improved weight loss and BMI (Grade A); however, use of this medication had a high rate of gastrointestinal side effects. Orlistat (under the trade name Xenical) is approved by the FDA for weight loss in pediatric patients ages 12 years and older in conjunction with a reduced calorie diet. In August 2009, the FDA released an early communication about an ongoing safety review regarding reports of liver-related adverse events in some patients taking orlistat. In May 2010, the orlistat labeling was updated to incorporate safety

information pertaining to the occurrence of rare post marketing cases of severe liver injury, including hepatic failure resulting in liver transplant or death.

- Dropout rates are substantial for all weight treatment programs.
- No studies defining an appropriate rate for weight loss in any age group were identified by the Guidelines evidence review. The 2010 *Dietary Guidelines for Americans* (*DGA*) recommends slowing weight gain while allowing normal growth and development. For those with BMI greater than or equal to the 95th percentile without comorbidities, both the American Medical Association, the Centers for Disease Control and Prevention, and the Maternal and Child Health Bureau (AMA/CDC/MCHB) Expert Committee and the American Academy of Pediatrics (AAP) recommend weight maintenance resulting in decreasing BMI as age increases. With BMI greater than or equal to the 95th percentile with comorbidities, the AMA/CDC/MCHB Expert Committee and the AAP recommend gradual weight loss not exceeding 1 pound per month in children ages 2–11 years or 2 pounds per week in adolescents (no grade).
- For adolescents with BMI far above 35 kg/m^2 and associated comorbidities, bariatric surgery on a research protocol, in conjunction with a comprehensive lifestyle weight loss program, improved weight loss, BMI, and other outcomes—such as IR, glucose tolerance, and cardiovascular (CV) measures—in a small case series (Grade D).

Evidence-Based Recommendations for Management of Child and Adolescent Patients with Overweight and Obesity

Grades reflect the findings of the evidence review.

Recommendation levels reflect the consensus opinion of the Expert Panel.

Birth–24 months	• No weight-for-height specific recommendations • Cardiovascular Health Integrated Lifestyle Diet (CHILD) 1 diet (see the NGC summary Nutrition and Diet) is recommended for pediatric care providers to use with their child and adolescent patients to reduce cardiovascular risk	
2–5 years	Identify children at high risk for obesity because of parental obesity and excessive BMI increase → Focused CHILD 1 diet and physical activity education • BMI percentile stable → Reinforce current program, followup in 6 months • Increasing BMI percentile → Registered dietitian (RD) counseling for energy-balanced diet, intensify physical activity change; 6-month followup	Grade B *Recommend*
	BMI 85th to <95th percentile:	
	Excess weight gain prevention with parents as focus for energy-balanced diet; reinforce physical activity recommendations × 6 months • Improvement in BMI percentile → Continue current program • Increasing BMI percentile → RD counseling for energy-balanced diet; intensify physical activity recommendations; 6-month followup	Grade D *Recommend*
	BMI ≥95th percentile:	
	Specific assessment for comorbidities*	Grade B *Strongly recommend*
	Family-based weight gain prevention with parents as focus; RD counseling and followup for energy-balanced diet; moderate-to-vigorous physical activity (MVPA) prescription; limit sedentary screen time; 3-month followup	Grade B *Recommend*
6–11 years	Identify children at increased risk for obesity because of parental obesity, change in physical activity +/- excessive gain in BMI for focused CHILD 1 diet/physical activity education • BMI percentile stable→ Reinforce current program, 6-month followup • Increasing BMI percentile→ RD counseling for energy-balanced CHILD 1 diet, intensified physical activity, 3-month followup	Grade B *Recommend*

	BMI 85th–<95th percentile:	
	Excessive weight gain prevention with parents as focus for energy-balanced diet; reinforce physical activity recommendations; 6-month followup • Stable/improving BMI percentile → Reinforce current program, 6-month followup • Increasing BMI percentile → RD counseling for energy-balanced CHILD 1 diet, intensified physical activity recommendations, 3-month followup	Grade D *Recommend*
	BMI ≥95th percentile:	
	Specific assessment for comorbidities.*	Grade B *Strongly recommend*
	BMI ≥95th percentile with no comorbidities:	
	Office-based weight loss plan: Family-centered program with parents as focus for behavior modification, (-) energy balance diet counseling by RD, prescription for increased MVPA, decreased sedentary time x 6 months • Improvement in BMI percentile/comorbidities→ Continue current plan • No improvement in BMI percentile→ Referral to comprehensive multidisciplinary lifestyle weight loss program	Grade A *Strongly recommend*
	BMI ≥ 95th percentile with co-morbidities, BMI ≥97th percentile, or progressive rise in BMI despite therapy:	
	Refer to comprehensive multidisciplinary weight loss program for intensive management x 6 months • Improvement in BMI percentile → Continue present program • No improvement in BMI percentile → Consider referral to another comprehensive multidisciplinary weight loss program	Grade A *Strongly recommend*
12–21 years	Identify adolescents at increased risk for obesity because of parental obesity, change in physical activity +/- excess gain in BMI for focused diet/physical activity education x 6 months • BMI/BMI percentile stable → Reinforce current program, 6-month followup • Increasing BMI/BMI percentile → RD counseling for energy-balanced CHILD 1 diet, intensified physical activity x 3 months	Grade B *recommend*
	BMI 85th–<95th percentile:	
	Excess weight gain prevention with adolescent as change agent for energy-balanced CHILD 1 diet, reinforced physical activity recommendations x 6 months • Improvement in BMI percentile→ Continue current program • Increasing BMI percentile→ RD counseling for energy-balanced weight control diet, intensified physical activity, 3-month followup	Grade B *recommend*
	BMI ≥95th percentile:	
	Specific assessment for comorbidities*	Grade B *Strongly recommend*
	BMI ≥95th percentile with no comorbidities:	
	Office-based weight loss plan: Family-centered with adolescent as change agent for behavior modification counseling, RD counseling for (-) energy-balanced diet, prescription for increased MVPA, decreased sedentary time x 6 months	Grade B *Strongly recommend*

	• Improvement in BMI/BMI percentile → Continue current program • No improvement in BMI/ BMI percentile → Referral to comprehensive multidisciplinary weight loss program with peers • No improvement in BMI/BMI percentile→ Consider initiation of medication (orlistat) under care of experienced MD x 6-12 months	
	BMI ≥95th percentile with comorbidities or BMI >35 kg/m^2:	
	Refer to comprehensive lifestyle weight loss program for intensive management x 6–12 months • Improvement in BMI/BMI percentile → Continue present program • No improvement in BMI/BMI percentile → Consider initiation of orlistat under care of experienced clinician x 6-12 months • BMI far above 35 kg/m^2 and comorbidities unresponsive to lifestyle therapy for >1 y → Consider bariatric surgery/referral to center with experience/expertise in procedures	Grade A *Strongly recommend*
*Comorbidities: Hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM)		

Definitions:

Evidence Quality for Grades of Evidence

Grade	Evidence
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the Guidelines' target population
B	Randomized controlled trials or diagnostic studies with minor limitations; genetic natural history studies; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, or reasoning from first principles (bench research or animal studies

Guidelines' Definitions for Evidence-Based Statements

Statement Type	Definition	Implication
Strong recommendation	The Expert Panel believes that the benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is excellent (Grade A or B). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade C or D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The Expert Panel believes that the benefits exceed the harms but the quality of the evidence is not as strong (Grade B or C). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should generally follow a recommendation but remain alert to new information and sensitive to patient preferences.
Optional	Either the quality of the evidence that exists is suspect (Grade D) or well-performed studies (Grade A, B, or C) show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set boundaries on alternatives; patient and family preferences should have a

Statement Type	Definition	Implication
No recommendation	There is both a lack of pertinent evidence (Grade D) and an unclear balance between benefits and harms.	Clinicians should not be constrained in their decision-making and should be alert to new published evidence that clarifies the balance of benefit versus harm; patient and family preferences should have a substantial influencing role.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Atherosclerotic cardiovascular disease
- Cardiovascular health
- Overweight
- Obesity

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Prevention

Screening

Treatment

Clinical Specialty

Cardiology

Family Practice

Internal Medicine

Nursing

Nutrition

Pediatrics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide comprehensive evidence-based guidelines addressing the known risk factors for cardiovascular disease (CVD)
- To assist all pediatric care providers in both the promotion of cardiovascular (CV) health and the identification and management of specific risk factors from infancy into young adulthood
- To provide recommendations to pediatric care providers on management of overweight and obesity in their patients

Target Population

- Children and adolescents in the general population and their parents/guardians
- Overweight and obese children and adolescents and their parents/guardians

Interventions and Practices Considered

1. Identifying children at high risk for obesity because of parental obesity, excessive body mass index (BMI) increase, or change in physical activity
2. Cardiovascular Health Integrated Lifestyle Diet (CHILD) 1 diet and physical activity education
3. Registered dietitian (RD) counseling for energy balanced diet
4. Specific assessment for comorbidities (hypertension, dyslipidemia, type 2 diabetes mellitus)
5. Family-based weight gain prevention or weight-loss with parents as focus
6. Family-centered weight loss plan with adolescent as change agent for behavior modification counseling
7. Moderate-to-vigorous physical activity (MVPA) prescription
8. Limiting sedentary screen time
9. Referral to comprehensive multidisciplinary weight loss program for intensive management
10. Medication (orlistat) under care of experienced medical doctor
11. Bariatric surgery referral

Major Outcomes Considered

- Weight loss
- Body mass index (BMI)
- Body fat
- Insulin resistance and glucose tolerance
- Blood pressure
- Atherosclerotic and other cardiovascular (CV) measures

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Evidence Review

The foundation of the systematic evidence review performed in support of the guideline development process was a series of critical questions related to cardiovascular disease (CVD) risk and prevention in youth. The questions encompassed defined risk factors, predefined outcome measures for each risk factor, and, most importantly, measures of CVD and target organ damage (TOD). Each of these elements was developed and refined through a review of the existing evidence by the Expert Panel. Additional information on the Critical Questions can be found in Table A-1 in Appendix A of the original guideline document.

To inform the identification of studies related to the critical questions, the Expert Panel held an inservice training with the contractor staff members who would be involved in overseeing the literature review to initiate the evidence review process. In addition, a series of group training sessions was held with the contractor staff at appropriate points throughout the process to clarify the scope of the review and expectations for supporting the production of high-quality, evidence-based guidelines.

Search Parameters

Based on the critical questions, risk factors, and types of CVD TOD of interest, search parameters were developed to identify published studies relevant to pediatric cardiovascular (CV) risk reduction. This process involved determining appropriate databases, dates, terms, and limits for the search, as described below.

Databases

Searches were performed in the following databases:

- PubMed/MEDLINE
- Cochrane Database of Systematic Reviews
- National Guideline Clearinghouse (NGC)

Searches were first conducted in PubMed/MEDLINE. Only unique studies from subsequent searches in the Cochrane database and NGC were retained for consideration (i.e., those studies that were not already captured in the initial PubMed/MEDLINE search).

In addition to these databases, a preliminary search of EMBASE was conducted. The great majority of studies identified in this preliminary search were also found in the other databases; therefore, it was determined that proceeding with a complete EMBASE search would not contribute significant additional information to the review.

The literature search allowed for further input by the Expert Panel to ensure that in-scope studies were not overlooked. Members of the Expert Panel contributed additional relevant studies based on their routine scanning of the literature. A supplementary literature search was also conducted to identify potentially relevant studies authored by members of the Expert Panel. Additional studies identified by these supplementary methods were included only if they met the same criteria for inclusion established for the primary evidence review.

Search Dates

Original searches in PubMed/MEDLINE, Cochrane, and NGC captured studies published between January 1, 1985, and December 31, 2006. Recognizing the timelag inherent in screening a large body of literature and developing evidence tables, the Expert Panel then called for an update of these searches to be conducted for the period between January 1, 2007, and June 30, 2007.

The Expert Panel established June 30, 2007, as the closing publication date for literature to be entered into the evidence review for these Guidelines. The Expert Panel recognized that, given the scope of these Guidelines and the nature of ongoing research in relevant areas, research findings might appear thereafter with the potential to have a material impact on one or more recommendations in the Guidelines. Therefore, to optimize the currency of the Guidelines, the Expert Panel sought, prospectively, to enable consideration of directly relevant, significant peer-

reviewed evidence that might appear after the closing date. During a conference call convened on January 21, 2008, the Expert Panel Science Team established the following criteria to guide the full Expert Panel's consideration of studies published after the closing date:

- Any peer-reviewed published study identified by a member of the Expert Panel, as part of his or her routine surveillance of the literature, that is directly relevant to the recommendations of the Expert Panel will be considered for inclusion.
- To be included by the Expert Panel as evidence, the corresponding Risk Factor Team, or the full Expert Panel if applicable at a broader level, must judge that the findings of such recently published studies have the potential for a material impact on the content or strength of the recommendations of the Expert Panel.
- Such studies must meet the same basic criteria for inclusion established for the primary evidence review.
- If there is a difference of opinion about inclusion of a study, a final decision will be made by the Expert Panel Chair.
- Studies that are selected for inclusion will undergo abstraction and full text review by the process established for the primary evidence review. To distinguish it from the body of evidence assembled via the systematic literature search conducted through the closing date of June 30, 2007, the body of evidence from any such more recent studies will be documented separately from the evidence tables comprising data from the original search.

Search Terms

To explore the most appropriate search strategy and examine the sensitivity and specificity of particular search terms, an initial search was done in PubMed/MEDLINE. This search used broad medical subject heading (MeSH) terms and text words for the concepts of pediatric/young adult populations, CVD/TOD, and the risk factors. Terms were combined using the Boolean operators "AND," "OR," and "NOT," which are described briefly in Table A–3 in Appendix A of the original guideline document.

The preliminary, broad search of PubMed/MEDLINE identified in excess of 1 million citations, signaling the need to refine the search terms to identify the most relevant ones. In consultation with the Expert Panel, key refinements in the search strategy were made, including (1) the use of major MeSH terms rather than MeSH terms, where appropriate; (2) the use of title and abstract terms rather than text words; (3) a reduction of the number of terms for each concept, leaving only the most central and essential terms; and (4) the application of excluded concepts to the search (in the form of "NOT" terms).

In the final search strategy, a combination of MeSH terms, major MeSH terms, and title and abstract terms was employed to identify the full range of relevant literature. Search terms were identified to capture studies in the pediatric and young adult target populations (ages 0–21 years) that also addressed CVD/TOD and/or at least one of the risk factors. Specific search terms are provided in Table A–9 in Appendix A of the original guideline document.

Search Limits

A set of limits was applied to the search to help refine the results to the most useful types of studies. The first level of basic search limits included:

- *Publication date*: published between January 1, 1985, and June 30, 2007
- *Language*: English language abstract or full text
- *Publication type*: no editorials, letters, comments, case reports, or non-systematic reviews

Search terms and field tags used to apply these limits to the search are provided in Table A–9 in Appendix A of the original guideline document.

In addition to these basic limits, search terms were used to exclude studies examining certain out-of-scope conditions. For example, during a preliminary review of the literature, many studies were identified that focused on various pediatric conditions such as Kawasaki disease, otitis media, or congenital heart diagnoses. Through consultation with the Expert Panel, search terms were developed for the most commonly observed out-of-scope conditions. Studies containing these terms were prospectively excluded by using the Boolean operator "NOT."

Search Results

Systematic Reviews, Meta-Analyses, Randomized Controlled Trials, and the Guidelines

After applying the initial limits and using terms to eliminate out-of-scope concepts, the number of results returned from the original literature searches was still in excess of 60,000 citations. Given the size of these literature results, the Expert Panel determined that part of the review would focus on certain study types that would be most useful to the Expert Panel during Guidelines development: systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), and guidelines. Search terms and field tags identifying study type were used to select these studies in the PubMed/MEDLINE database.

Secondary studies, such as SRs and MAs, compile results from primary analyses and, in some cases, review of these study types may lessen the

need to examine primary evidence on a topic. However, given the breadth of this evidence review, there were no instances in which an SR or MA captured the entire scope of interest of a critical question; therefore, this review depended on RCTs as an important source of primary data on relevant interventions.

The schematic in Figure A–1 in Appendix A of the original guideline document presents a simplified, high-level depiction of how the key search concepts were combined to achieve the overall search strategy.

In childhood, much of the evidence linking risk factors to atherosclerosis comes from epidemiologic studies. Therefore, in addition to including SRs, MAs, RCTs, and guidelines in the review, the Expert Panel determined that it was necessary for the evidence review to include major epidemiologic studies selected by the Expert Panel. These studies represent landmark longitudinal and natural history studies and other sentinel work that have provided important information and insight about atherosclerosis and CV risk in children. The major observational studies that were included are listed in Table A–4 in Appendix A of the original guideline document.

A separate targeted search of PubMed/MEDLINE was conducted to identify literature relevant to these major studies related to the risk factors for the inclusive period of the evidence review from January 1, 1985, to June 30, 2007. The observational literature was also updated by the Expert Panel using the same criteria developed for the classic evidence review. Terms used to conduct this search are provided in Table A–10 in Appendix A of the original guideline document. National Heart, Lung and Blood Institute (NHLBI) staff reviewed the titles and then the abstracts for studies to be included based on the 14 risk factors under review. When a longitudinal study reported results of the same variables at increasing intervals from the beginning of the observational period, the most recent report detailing the longest period of observation was selected for inclusion. Duplicate reports of the same results were excluded. The observational studies to be included in the evidence review were selected by the Expert Panel Risk Factor Teams.

Additional References

In an evidence-based review, studies included are generally limited to RCTs, SRs, and MAs. In addition to the epidemiologic studies described above, Expert Panel members also included studies that provided important information for each risk factor, defining the context in which the Guidelines' recommendations were developed. These references are not part of the evidence tables but are identified sequentially throughout the text and will be listed in Appendix B of the original guideline document by section in numeric order, as identified in the text. Of particular importance were studies of genetic conditions impacting CV risk status and natural history studies of specific diseases known to be associated with accelerated atherogenesis.

Inclusion and Exclusion Criteria

In preparation for review of the literature, inclusion and exclusion criteria were developed by the Expert Panel. These criteria outlined additional boundaries for the review. Certain criteria were applied only by the Expert Panel, given that judgments regarding the application of these criteria required relevant clinical expertise.

Inclusion Criteria

- Pertained to at least one of the specified risk factors and measured at least one of the predetermined outcomes
- Related to at least one of the critical questions
- Focused on the target population (ages 0–21 years)
    - For longitudinal studies and other studies with extended followup periods, the population was required to be in this age range at initiation, and this subcohort could be identified in subsequent analyses.
    - For the Guidelines, the target population was required to include at least part of this age range.
- Conducted in Europe, North America, Australia, New Zealand, Japan, or Israel
- In 2004, an NHLBI-appointed Task Force published *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*. This report included a complete review of the current evidence on this subject and detailed recommendations for managing blood pressure (BP) throughout childhood. These recommendations were used as the basic recommendations for BP management for these Guidelines and are considered complete until 2003 when the review for the report ended. The literature review for BP, therefore, was limited to January 1, 2003, through June 30, 2007; selected studies from 2008 identified by the Expert Panel that met all the criteria for inclusion in the evidence review were also included.

Exclusion Criteria

- Any study not meeting the above requirements was excluded from the review.
- Studies that otherwise met inclusion criteria but that were found, upon examination, to have measured risk factors in only an incidental way or as part of assessing the safety of an intervention were excluded. For example, a study of an asthma medication might measure BP to

ensure that there were no adverse effects of the medication. Such studies that measured in-scope outcomes that were not linked to a risk factor condition were excluded from the review.

- Duplicate reports of findings based on the same original studies were generally excluded. For instances in which a series of studies (typically longitudinal studies or large RCTs) reported results for the same outcome measures over a period of time, the most recent studies and main results of trials were typically retained and older studies were excluded. These determinations were made individually during the review of each study.
- Studies that did not meet basic internal/external validity standards (e.g., as a result of narrowly defined patient population) were excluded.
- Studies that addressed the target population, often as part of a broader age range, but did not provide findings specific to patients in the target age range were excluded.
- Studies were excluded that on closer inspection were found not to be SRs, MAs, RCTs, guidelines, or reports from the selected epidemiologic studies.
- Studies were excluded that had an insufficient number of patients at followup to draw meaningful conclusions.
- Studies conducted in patients with diabetes focused on interventions that were related exclusively to glycemic control were excluded.
- For studies that focused on smoking as a risk factor, those that reported on interventions related to policymaking or merchant behavior were excluded.

During the review process, inclusion and exclusion criteria were modified to account for topics identified as irrelevant and certain included topics were clarified. Throughout this process, abstractors and the Expert Panel were in close contact to resolve questions regarding the application of inclusion/exclusion criteria to individual studies.

Literature Review Process

After completing electronic searches in each database, a total of 11,231 SRs, MAs, RCTs, guidelines, and major observational studies were identified for review. The distribution of search results by database and study type is presented in Table A–5 in Appendix A of the original guideline document.

Abstracts and citations for these studies were compiled and organized using Reference Manager.

Figure A–2 in Appendix A of the original guideline outlines the phases of the literature review process and the number of studies excluded at each stage. Throughout each review phase the Expert Panel provided guidance regarding the appropriate application of inclusion and exclusion criteria.

Following the review of titles and abstracts, trained abstractors conducted a full-text review of the studies and excluded additional studies. NHLBI staff also reviewed the full text of these studies and identified additional studies to exclude. Following the full-text review phase, an additional 200 studies were excluded. Citations for studies excluded at the full-text level are provided online, along with the complete evidence tables.

In addition to a review of the studies captured through the literature search process (i.e., studies published between January 1, 1985, and June 30, 2007), the NHLBI and the Expert Panel identified an additional 29 relevant studies that were published after June 30, 2007, for inclusion in the review.

Number of Source Documents

At the end of the review process, a total of 664 studies were included for review—including 51 systematic reviews, 34 meta-analyses, 304 randomized controlled trials, 84 guidelines, and 191 observational studies.

The Expert Panel's evidence review for overweight and obesity included a large number of studies: 30 systematic reviews, 12 meta-analyses, 121 randomized controlled trials (RCTs), and 47 observational studies.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Quality for Grades of Evidence

Grade	Evidence
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the Guidelines' target population
B	Randomized controlled trials or diagnostic studies with minor limitations; genetic natural history studies; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, or reasoning from first principles (bench research or animal studies

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Collection and Quality Control

Systematic Reviews, Meta-Analyses, Randomized Controlled Trials, and Guidelines

To capture information from in-scope studies, Excel tables were developed and used for data abstraction of each study type (i.e., systematic review [SR], meta-analysis [MA], randomized controlled trial [RCT]). Through discussion the Expert Panel, the types of information collected and the format of the tables were refined. Data collected in the abstraction tables included basic information about the study (e.g., year of publication), objective, patient population, intervention and comparator/control (if applicable), outcomes measured, and results. Data abstracted varied by study type. A complete list of data fields and definitions for these fields is provided through the National Heart, Lung and Blood Institute (NHLBI) Web site.

To complete the data abstraction tables, trained abstractors reviewed full-text versions of each in-scope study. Two reviewers examined each full-text study; the first reviewer abstracted the appropriate data from each study, while the second reviewer concentrated on ensuring the accuracy and quality of data entered by the first reviewer as part of a thorough quality control process. For RCTs, contractor staff abstracted information for specific columns, including basic information about the study, objective, patient population, intervention and comparator/control (if applicable), and outcomes measured. For SRs and MAs, the contractor staff abstracted information for all columns. For observational studies, contractor staff abstracted the basic informational data, but full-text review and data entry were performed by NHLBI staff.

After data abstraction by the contractor, the data abstraction tables were submitted to the NHLBI and the Expert Panel for review and/or completion of abstraction. For all study types, Expert Panel members were responsible for verifying data entered by the contractor. For RCTs, Expert Panel members and NHLBI staff selected the outcome variables to be abstracted and entered the results in the evidence tables, as well as recorded study results and conclusions. To facilitate this process, studies were forwarded to the relevant subcommittee within the Expert Panel, according to the primary risk factor of focus. For example, a study that examined the use of an intervention to improve cholesterol levels would have been forwarded to the subcommittee on lipids. Study reviews were rotated to ensure that each was reviewed by two subcommittee members. Subcommittee members completed abstraction of established columns and, in several cases, requested the addition of extra columns in the evidence tables to capture more specific information pertaining to the risk factor of interest. When Expert Panel members were not in agreement regarding such matters as study relevance or abstraction of specific data, these matters were brought to the Expert Panel Chair for resolution.

In addition to basic information about study design and results, aspects of study quality were considered by the Expert Panel during data abstraction. A customized quality grading system was developed to support the Expert Panel's interpretation of individual studies, particularly with regard to methodology and study design considerations. This novel grading system, the development of which drew largely from several existing grading schemes, was incorporated into the electronic data abstraction tables. The system used an algorithm that generated a quality grade for individual RCTs, according to the criteria outlined in Tables 11 and 12 in Appendix A of the original guideline document. SRs, MAs, and observational studies did not receive an individual quality grade.

After completion of data abstraction, evidence tables displaying key study information were developed from the data abstraction tables using Excel

for use by the Expert Panel. These standard evidence tables were then sorted in a customized way for each subcommittee, so as to best support the Guidelines development process. Final evidence tables for all included SRs, MAs, RCTs, and observational studies are provided online at http://www.nhlbi.nih.gov/guidelines/cvd_ped/index.htm.

Although reports of guidelines were captured as part of the literature search, they were not incorporated into evidence tables. Instead, the guidelines were reviewed for relevance, and those that were in scope were categorized according to the risk factor(s) addressed. A list of the in-scope guidelines was made available to Expert Panel members for their reference; full-text versions were made available as needed. Citations for in-scope guidelines, by risk factor, are also provided online.

Major Observational Studies

Excel tables were also developed for the epidemiologic observational studies, with basic information about each study entered into tables by skilled abstractors from contractor staff. Full-text review and abstraction of each study were performed by NHLBI staff, including identification of outcome variables and review of results and conclusions. These tables were then reviewed by Expert Panel members, who selected 191 studies as relevant to the evidence review. The tables were primarily categorized by risk factor and then sorted using the terms developed by the relevant Risk Factor Teams for inclusion in the review. Expert Panel members added additional relevant reports from any of these observational studies that appeared after conclusion of the formal review. The evidence tables for the observational studies are also included on the NHLBI Web site.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Expert Panel and Subcommittee Discussion

Following establishment of the Expert Panel, in-person meetings were held in October 2006, February 2007, June 2008, and October 2008. These meetings enabled Expert Panel members to discuss key elements of the systematic evidence review, consider the approach and scope of the Guidelines, and review and refine the Guidelines' recommendations.

To facilitate discussion of the evidence related to particular risk factors, multiple subcommittee conference calls were held from February to December 2008, along with a continuous electronic correspondence. Across the seven subcommittees, more than 500 conference calls were completed. During these calls, subcommittee members established processes for developing and finalizing the Guidelines' recommendations for each risk factor and progressively shaped the final recommendations in the Guidelines. A SharePoint Web site was created to enable subcommittee members to share draft recommendations.

Established Parameters for Guidelines Recommendation Development

The Expert Panel adopted an evidence grading system from the American Academy of Pediatrics (AAP) to assess the quality of the body of evidence as a whole and the evidence in support of particular statements. The grading system is shown in the "Rating Scheme for the Strength of the Evidence" field; it was modified by the addition of genetic natural history studies to the grade B evidence category; an example of a genetic natural history study is the development of atherosclerosis in a child with homozygous familial hypercholesterolemia who has severely elevated cholesterol levels from birth. Studies of such genetic conditions are believed to represent a natural intervention and to function as surrogates for a specific lifelong risk exposure. Genetic variation shares features with random assignment in clinical trials in that the variation occurs by chance within a society and the presence of the genetic variation does not alter exposure to environmental or other factors. Drawing from the same AAP system, the "Rating Scheme for the Strength of the Recommendations" field depicts the Guidelines' definitions for evidence-based statements.

The Expert Panel also developed a definition of consensus to guide decision making regarding Guidelines recommendations within the subcommittees and among the full Expert Panel. The final definition included the following elements:

- Committee deliberations regarding a given recommendation generally reflected deference to the expert risk factor subcommittee that was originally charged with critically appraising the evidence and drafting the recommendation.
- Voting was "in support of" or "opposed to" a recommendation.
- Agreement by at least 80 percent (or 11 of 14 members) of the Expert Panel constituted a strong consensus. A recommendation with this level of agreement is presented in the Guidelines as a consensus of the Expert Panel. However, discussion of the issues in the Guidelines document may address areas of difference.

- A proposed recommendation that was supported by less than 60 percent (or less than 8 of 14 members) of the Expert Panel was not included in the Guidelines. However, review of the subject could be included in the discussion for that risk factor area.
- Agreement by 60–80 percent (9 or 10 of 14 members) of the Expert Panel constituted a moderate consensus in support of the recommendation. A recommendation with this level of agreement was presented with that language in the Guidelines and accompanied by discussion of the conflicting issues. In developing the discussion in support of a recommendation, the actual vote of the Expert Panel was considered.

In considering the various pediatric age groups covered by the Guidelines' recommendations, the Expert Panel agreed to formulate the Guidelines' recommendations according to the chronological timetable used by the AAP *Bright Futures* program:

- Preconception/prenatal
- 0–12 months
- 1–4 years
- 5–10 years
- 11–17 years
- 18–21 years

Studies were not always specific to an age group, and the Expert Panel used judgment in determining how those studies informed age-specific recommendations.

Completion of the Guidelines

At the final full Expert Panel meeting in October 2008, the Expert Panel reviewed each recommendation proposed by each subcommittee in detail. According to the established definition of consensus, the Expert Panel agreed on a complete set of recommendations and supporting text in the draft Guidelines report.

Rating Scheme for the Strength of the Recommendations

Guidelines' Definitions for Evidence-Based Statements

Statement Type	Definition	Implication
Strong recommendation	The Expert Panel believes that the benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is excellent (Grade A or B). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade C or D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The Expert Panel believes that the benefits exceed the harms but the quality of the evidence is not as strong (Grade B or C). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should generally follow a recommendation but remain alert to new information and sensitive to patient preferences.
Optional	Either the quality of the evidence that exists is suspect (Grade D) or well-performed studies (Grade A, B, or C) show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set boundaries on alternatives; patient and family preferences should have a substantial influencing role.
No recommendation	There is both a lack of pertinent evidence (Grade D) and an unclear balance between benefits and harms.	Clinicians should not be constrained in their decision-making and should be alert to new published evidence that clarifies the balance of benefit versus harm; patient and family preferences should

Statement Type	Definition	Implication
		have a substantial influencing role.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

In April 2009, a draft version of the Guidelines was circulated to other National Institutes of Health (NIH) Agencies and multiple professional organizations for review and comment. The draft version was also posted on the National Heart, Lung and Blood Institute (NHLBI) Web site for public comment for a 30-day period from June 19 to July 20, 2009. In total, the Expert Panel considered more than 1,000 comments from more than 50 reviewers, and individual responses were developed for more than 1,000 comments. The draft version of the Guidelines also underwent a separate review by the NHLBI and the U.S. Department of Health and Human Services (HHS). After considering all comments, consistent with applicable Federal requirements, the Expert Panel made appropriate revisions to the draft report. The summary report was published in final form November 11, 2011.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The promotion of cardiovascular (CV) health and the identification and management of specific risk factors from infancy into young adult life
- Improvement in weight status and decrease in body fatness have been shown to be associated with decreases in systolic and diastolic blood pressures (BPs), total cholesterol (TC), low-density lipoprotein cholesterol (LDL–C) and/or triglycerides (TG), insulin resistance, and inflammatory markers. Subclinical vascular changes indicative of atherosclerosis have been demonstrated in overweight and obese children; exercise and weight loss have been shown to result in significant improvement in these measures.

Potential Harms

In August 2009, the U. S. Food and Drug Administration (FDA) released an early communication about an ongoing safety review regarding reports of liver-related adverse events in some patients taking orlistat. In May 2010, the orlistat labeling was updated to incorporate safety information pertaining to the occurrence of rare postmarketing cases of severe liver injury, including hepatic failure resulting in liver transplant or death.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Overweight and obesity. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. p. 282-321. [132 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011

Guideline Developer(s)

National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency [U.S.]

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United States Government

Guideline Committee

Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents

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Refer to the original guideline document for members of the National Heart, Lung, and Blood Institute staff and for names of the contractor support.

Financial Disclosures/Conflicts of Interest

Expert panel members disclosed relevant financial interests to each other prior to discussions. The following financial interests are reported in the publication in the *Journal of Pediatrics*:

Dr. Benuck, Dr. Christakis, Dr. Dennison, Dr. O'Donnell, Dr. Rocchini, and Dr. Washington have declared no relevant relationships.

Dr. Daniels has served as a consultant for Abbott Laboratories and Merck, Schering-Plough. He has received funding/grant support for research from the NIH.

Dr. Gidding has served as a consultant for Merck, Schering-Plough. He has received funding/grant support for research from GlaxoSmithKline.

Dr. Gillman has given invited talks for Nestle Nutrition Institute and Danone. He has received funding/grant support for research from Mead Johnson, Sanofi-aventis and the NIH.

Dr. Gottesman has served on the Health Advisory Board, Child Development Council of Franklin County. She was a consultant to Early Head Start for Region 5B. She has written for iVillage and taught classes through Garrison Associates for the State of Ohio, Bureau of Early Intervention Services and Help Me Grow program. She has received funding/grant support for research from NIH.

Dr. Kwiterovich has served as a consultant or advisory board member for Merck, Schering-Plough, Pfizer, Sankyo, LipoScience and AstraZeneca. He has served on speaker bureaus for Merck, Schering-Plough, Pfizer, Sankyo, Kos and AstraZeneca. He has received funding/grant support for research from Pfizer, Merck, GlaxoSmithKline, Sankyo and Schering-Plough.

Dr. McBride has served as a consultant or advisory board member for Bristol-Myers Squibb, and Merck. He has served on speakers bureaus for Kos, Merck and Pfizer. He declared no relevant relationships since July 2007.

Dr. McCrindle has been a consultant for Abbott, Bristol-Myers Squibb, Daichii Sankyo and Roche. He owns stock in CellAegis. He reports funding/grant support for research from AstraZeneca, Sankyo, Merck, Schering-Plough and the NIH.

Dr. Urbina reports funding/grant support for research from Merck, Schering-Plough, Sankyo and the NIH.

Dr. Van Horn has provided advice to Chartwells School Food Service. She has received funding/grant support for research from General Mills and the NIH.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Heart, Lung, and Blood Institute (NHLBI) Web site .

Print copies: Available from the NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: nhlbiic@dgsys.com.

Availability of Companion Documents

The following are available:

- Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Summary report 2011. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. 125 p. Electronic copies: Available in Portable Document Format (PDF) from the National Heart, Lung, and Blood Institute Web site .
- Evidence tables. Electronic copies: Available in PDF from the National Heart, Lung, and Blood Institute Web site .

Patient Resources

Various resources for the public about heart and vascular diseases are available from the National Heart, Lung and Blood Institute Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on July 12, 2012. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs.

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